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Meconium ileus in the absence of cystic fibrosis

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Abstract

Although meconium ileus in the absence of cystic fibrosis is considered a rare event, it was found that eight of 37 (21·6%) newborn infants with meconium ileus had no laboratory or clinical evidence of cystic fibrosis.

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Meconium ileus is the earliest clinical manifestation of cystic fibrosis in 10–20% of affected patients (13·4% at this clinic),[1] but it is a rare phenomenon in patients who do not have this condition. We report eight neonates with meconium ileus, who had no clinical or laboratory evidence of cystic fibrosis.

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Patients, methods, and results

During the six year period, 1986–91, 37 neonates with meconium ileus were seen at the Hospital for Sick Children, Toronto, Eight (four boys) of these 37 patients (21·6%) were subsequently shown to have no laboratory evidence of cystic fibrosis, and they form the basis of this report.

The patients' characteristics are summarised in the table. Four of the eight infants were delivered prematurely (that is, less than 37 weeks' gestation), three of whom required intubation and mechanical ventilation at birth. Maternal complications included polyhydramnios (patients 4 and 7) and pre-eclampsia (patient 6), but there was no family history of cystic fibrosis. All presented with signs of intestinal obstruction with abdominal distension (with the exception of patient 5), and failure to pass meconium, and four infants developed ileal perforation. All except patient 5 required laparotomy, and three infants required bowel resection. Complications noted at surgery included ileal perforation, meconium peritonitis, meconium pseudocysts, ileal volvulus, and ileal atresia (table). Histopathology of the surgically resected specimens of small bowel revealed necrosis and haemorrhage, but lesions typical of cystic fibrosis[2] or Hirschsprung's disease were not identified. Pilocarpine iontophoresis sweat chloride tests were normal on two occasions in all patients. Genetic studies were performed on six subjects, none of whom had the ΔF_{508} deletion, which is present in 68% of patients with cystic fibrosis at this clinic.[3] Six of the eight infants had a favourable outcome and developed no gastrointestinal, nutritional, or pulmonary complications.

Patient 2, who was born at 30 weeks'gestation, required mechanical ventilation for 17 days and developed mild bronchopulmonary dysplasia. Patient 6 required continuous mechanical ventilation for 106 days for the respiratory distress syndrome, which resulted

Clinical data of the eight patients

Patient No	*Sex*	*Gestational age (weeks)*	*Age at presentation*	*Birth weight (g)*	*Clinical presentation*	*Abdominal radiograph*
1	M	36	Day 2	2730	Formula feeds for 24 hours, abdominal distension, vomiting (bilious drainage by nagogastric tube). No meconium passed after 24 hours	Distended loops with air-fluid levels, no air in colon. Barium enema: microcolon, ? distal small bowel atresia
2	M	30	Day 3	730	Ventilated for RDS (17 days): not fed, developed abdominal distension, periumbilical erythema. No meconium passed by day 2.	Dilated loops (day 1), free air in the abdomen (day 3)
3	F	40	At birth	3210	Not fed, developed abdominal distension. No meconium passed; bilious drainage by nasogastric tube	No abdominal gas; microcolon; calcification in RIF. ? Meconium cyst
4	M	35	Day 2	2630	Low Apgar scores—ventilated for 24 hours: not fed, developed ascites and raised serum transaminase values on day 2. No meconium passed by day 2	No abdominal gas. Barium enema: malrotation, proximal dilation of small bowel with free air in the abdomen
5	F	40	12 hours	3120	Breast fed, bilious vomiting. No meconium passed	Barium meal: ?mass in RIF, barium enema: patchy filling defects in colon and the last 10 cm of ileum
6	F	27	Day 2	870	Ventilated for RDS (106 days): not fed, abdominal distension. No meconium passed by day 3	Dilated bowel loops. Barium enema: microcolon
7	F	39	At birth	3500	Not fed, abdominal distension, bilious gastric aspirate	Air bubble in the stomach, no air in the rest of the bowel. Barium enema: proximal bowel dilatation microcolon
8	M	40	7 hours	3000	Breast fed, abdominal distention, bilious vomiting	Paucity of air in the abdomen, free air under diaphragm

BPD=bronchopulmonary dysplasia; RDS=respiratory distress syndrome; RIF=right iliac fossa.

in the development of bronchopulmonary dysplasia. Despite irrigation of the bowel with *N*-acetylcysteine at laparotomy, no meconium was passed, and further surgery was required at day 14 of life after a rectal perforation. Several attempts at extubation failed and this baby died at 4 months of age from lower respiratory infection, superimposed on chronic lung disease. With the exception of patients 2 and 6, all infants in our series had normal chest radiographs.

Discussion

Although all of the newborns described presented with meconium obstruction of the terminal ileum, none had clinical or laboratory evidence of cystic fibrosis. Meconium intestinal obstruction in the neonatal period can be due to three conditions (1) meconium ileus; (2) meconium plug syndrome; and (3) meconium disease (inspissated meconium syndrome).

Meconium ileus is due to mechanical obstruction of the terminal ileum with thick, viscid meconium, and in about 50% of cases is complicated by volvulus, atresia, or meconium peritonitis.[4] In cystic fibrosis, meconium ileus is thought to result from abnormal mucus production in the intestine[2] and/or impaired pancreatic enzyme or fluid secretion.[5] Meconium ileus rarely occurs in infants without cystic fibrosis,[6] but has been reported with pancreatic duct stenosis,[7] partial pancreatic aplasia,[8] ileocaecal atresia[9] as a familial condition[10 11] and a functional disorder in preterm babies.[12] The meconium plug syndrome has also been reported in cystic fibrosis.[13] In this condition, transient obstruction of the distal colon occurs, although meconium plugs in the ileum may cause complications, requiring surgery.[14] Meconium disease has been described in premature infants with very low birth weight and is not associated with cystic fibrosis.[15] In this condition meconium plugs are found in the distal ileum and proximal colon and the resulting obstruction can generally be relieved by enemas.

Although overlap between the three causes of meconium obstruction may occur, the cases we report most closely resemble meconium ileus.[4] In addition, typical complications of meconium ileus occurred in five of our cases, necessitating surgical intervention. However, sweat tests were negative in all of our patients, none had clinical or laboratory evidence of pancreatic insufficiency, and the most common deletion associated with cystic fibrosis (ΔF_{508})[3] was not present in the six infants who had genetic studies. We feel confident, therefore, that our patients did not have cystic fibrosis.

Meconium ileus in the absence of cystic fibrosis is considered a rare event and has been reported in only a few cases,[16–18] sometimes as a familial condition.[10 11] However, 21·6% of our patients with meconium ileus did not have cystic fibrosis. Although the exact cause of meconium ileus is unclear, four out of eight of the babies described were born prematurely (<37 weeks' gestation), three of whom required mechanical ventilation. It is possible that reduced intestinal motility may have contributed to the development of meconium ileus in these infants.

In summary, our report indicates that a significantly greater number of newborn infants with meconium ileus will not have cystic fibrosis than has been previously described. Definitive parental counselling should, therefore, be delayed until accurate sweat chloride tests can be obtained.

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Operative findings	*Genetic analysis*	*Treatment*	*Outcome*
Meconium ileus, meconium obstructing the ileocaecal valve. No atresia	Not done	Bowel flushed with *N*-acetylcysteine	No complications. Normal faecal fat and bentiromide study
Meconium ileus with perforation of mid-ileum	Negative for ΔF_{508}	5 cm ileal resection and end to end anastomosis	No nutritional or gastrointestinal problems. Serum trypsinogen normal. Mild BPD
Meconium peritonitis. Meconium cyst: ileal atresia with perforation	Negative for ΔF_{508}	10 cm small bowel resection, and ileostomy	No nutritional, gastrointestinal, or respiratory problems
Meconium ileus with mid-ileal volvulus and perforation	Not done	10 cm small bowel resection with end to end anastomosis and irrigation of distal bowel with *N*-acetylcysteine	Jejenostomy required for small bowel dehiscence. No nutritional or respiratory problems
No surgery	Negative for ΔF_{508}	*N*-acetylcysteine by nasogastric tube and enema	No nutritional or respiratory problems. Normal faecal fat study and serum trypsinogen
Meconium ileus, microcolon	Negative for ΔF_{508}	Bowel flushed with *N*-acetylcysteine	Severe BPD. Rectal perforation day 14. Died from respiratory failure at 4 months
Segmental ileal volvulus at mid-ileum meconium cyst, and associated ileal atresia	Negative for ΔF_{508}	Meconium cyst resection, side to end anastomosis	Normal trysinogen value
Perforated distal ileum, meconium peritonitis	Negative for ΔF_{508}	Ileostomy, no bowel resection	Raised trypsinogen value

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